UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte SUZANNE DE LA MONTE and JACK R. WANDS

Appeal No. 2005-0807[1]
Application No. 09/380,203

HEARD: April 19, 2005

Before WILLIAM F. SMITH, SCHEINER and GRIMES, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of claims 1-3, 5, 6, 10-13, 35 and 44-47. Claims 39-43 and 49 have been allowed, and claims 36-37 are objected to.

AD7c-NTP cDNA, isolated from an Alzheimer's disease [AD] brain expression library, encodes a protein which is "expressed in neurons, and over-expressed in brains with AD." Specification, page 17. According to appellants, "*In situ* hybridization and immunostaining studies localized AD7c-NTP gene expression in neurons, and confirmed the over-expression associated with AD neurodegeneration . . . suggest[ing] that abnormal AD7c-NTP gene expression is associated with AD neurodegeneration . . . [and

[1] This appeal is related to an appeal in Application Serial No. 09/964,678 (Appeal No. 2004-2135). We have considered the two appeals together.

that] abnormal expression of AD7c-NTP is a phenotype associated with Alzheimer's disease." Id., page 18. AD7c-NTP has been observed to "induce neuritic sprouting, nerve cell death, nerve cell degeneration, neurofibrillary tangles, and/or irregular swollen neurites in a host which expresses the [protein]." Id., pages 18-19.

The claims on appeal are directed a DNA construct comprising AD7c-NTP DNA (i.e., SEQ ID NO:1) or a DNA molecule which is at least 90% homologous to SEQ ID NO:1, wherein the DNA molecule is under the control of a heterologous neuro-specific promoter, and codes for a protein that has an activity of AD7c-NTP when over-expressed in neuronal cells. In addition, the invention is directed to a method of using host cells containing the construct to screen candidate drugs "potentially useful for the treatment or prevention of" Alzheimer's disease.

Claims 1, 5 and 10 are representative of the subject matter on appeal:

1. A DNA construct, which comprises the DNA molecule of SEQ ID NO:1 or a DNA molecule which is at least 90% homologous thereto, wherein said DNA molecule is under control of a heterologous neuro-specific promoter, and wherein said DNA molecule codes for a protein that has an activity of AD7c-NTP when over-expressed in neuronal cells.

5. A host cell transformed with the DNA construct of claim 1.

10. An *in vitro* method for screening a candidate drug that is potentially useful for the treatment or prevention of Alzheimer's disease, neuroectodermal tumors, malignant astrocytomas, or glioblastomas, said method comprising:
(a) contacting a candidate drug with the host cell of claim 5, and
(b) detecting at least one of the following:
(i) the suppression or prevention of expression of the protein coded for by the DNA construct of said host cell;
(ii) the increased degradation of the protein coded for by the DNA construct of said host cell; or
(iii) the reduction of frequency of at least one of neuritic sprouting, nerve cell death, degenerating neurons, neurofibrillary tangles, or irregular swollen neurites and axons in said host cell, wherein said host cell is a neuronal cell;
due to the drug candidate compared to a control cell line which has not contacted the candidate drug.

DISCUSSION

Claims 1-3, 5, 6, 10 and 12-13 stand rejected under the first paragraph of 35 U.S.C. § 112, as lacking adequate written description. Claims 1-3, 5, 6, 10-13, 35 and 44-47 stand rejected under the first paragraph of 35 U.S.C. § 112, as lacking enablement.

We reverse these rejections.

Written Description

According to the examiner, "[t]he specification provides sufficient description of SEQ ID NO: 1 . . . [which] codes for an AD7c-NTP protein" (Answer, page 4), but not for "a genus of DNA molecules with 90% homology to SEQ ID NO:1 that codes for a protein that has an activity of AD7c-NTP when over expressed in neuronal cells" (id.). The examiner asserts that "[t]he skilled artisan cannot envision the detailed structure of a genus of a DNA molecule, which displays at least 90% homology to SEQ ID NO:1 that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification." Id., pages 5-6.

"The 'written description' requirement serves a teaching function, . . . in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.'" University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 922, 69 USPQ2d 1886, 1891 (Fed. Cir. 2004) (citation omitted). Another "purpose of the 'written description' requirement is . . . [to] convey with reasonable clarity to those skilled in the art that, as of the filing date [ ], [the applicant] was in possession of the invention." Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-

64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See also Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1329, 63 USPQ2d 1609, 1617 (Fed. Cir. 2002). The requirement is satisfied when the specification "set[s] forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896. Whether or not a specification satisfies the requirement is a question of fact, which must be resolved on a case-by-case basis (Vas-Cath, 935 F.2d at 1562-63, 19 USPQ2d at 1116), and it is the examiner's "initial burden [to] present[ ] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims" (In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)).

"[A]pplicants have some flexibility in the 'mode selected for compliance' with the written description requirement" (University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896); it is well settled that actual reduction to practice is not necessary to satisfy the requirement (id., at 926, 69 USPQ2d at 1894). In University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), the court discussed the application of the written description requirement to inventions in the field of biotechnology, stating that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed

> by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. at 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material" (id.), but "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

Subsequently, the court clarified that "[not] all functional descriptions of genetic material fail to meet the written description requirement," for example, "the written description requirement would be met for [a claim] . . . if the functional characteristic . . . were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed." Enzo Biochem, 296 F.3d at 1324-25, 63 USPQ2d at 1613.

Here, all of the polynucleotides in the claimed genus have a certain amount of structural commonality (all are "at least 90% homologous" to SEQ ID NO:1 (the cDNA encoding AD7c-NTP)), and all encode proteins which have at least one defined functional characteristic, "an activity of AD7c-NTP when over-expressed in neuronal cells." The specification describes methods of isolating DNA molecules at least 90% homologous to SEQ ID NO:1; specific activities of AD7c-NTP; and assays to confirm those activities. Specification, pages 18-20, e.g. Again, as explained in Lilly, a genus of polynucleotides can be described by a representative number of polynucleotides,

defined by sequence, or sharing common structural features which constitute a substantial portion of the genus; and, as explained in Enzo, a genus may be described by means of a functional characteristic coupled with a disclosed correlation between that function and a known or disclosed structure.

Whether the level of disclosure in the specification would have allowed one skilled in the art to recognize that the inventor invented what is claimed is a question of fact. The USPTO has summarized a number of factors to be considered in making this determination; they include "the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." Guidelines for Examination of Patent applications Under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001). "Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." Id.

Rather than providing an analysis of these or any other factors, the examiner simply asserts that "an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the claimed invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of DNA molecules that must exhibit the disclosed biological functions as contemplated by the specification." Answer, pages 4-5.

This conclusory statement is insufficient to meet the examiner's initial burden of establishing that one skilled in the art would not have recognized that appellants were in possession of what is claimed. Accordingly, the rejection is reversed.

Enablement

With respect to claims 1-3, 5, 6 and 35, the examiner concludes that "the specification is enabling only for a DNA construct[ ] which comprises the DNA molecule of SEQ ID NO: 1 . . . and does not reasonably provide enablement for a DNA molecule which is at least 90% homologous to SEQ ID NO: 1 . . . wherein said DNA molecule codes for a protein that has an activity of AD7c-NTP when over-expressed in neuronal cells" (Answer, page 6). According to the examiner, "it would [have] required undue experimentation . . . to arrive at other DNA molecules with 90% homology to SEQ ID NO:1 [ ] having [AD7-NTP] activity when over-expressed in neuronal cells" (id., page 8).

"The first paragraph of 35 U.S.C. § 112 requires, inter alia, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.' In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).[2] That some experimentation may be required is not fatal; the issue is whether the amount of experimentation is 'undue.'" In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (emphasis in original). Nevertheless, "[w]hen rejecting a claim under the enablement requirement of section 112," it is well settled that "the PTO

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> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims (footnote omitted).
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> In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Thus, the issue here is not whether appellants have established that the disclosure is enabling for the claims, rather, the issue is whether the PTO has met its "initial burden of setting forth a reasonable explanation as to why" it is not. With this in mind, we consider the reasons given in support of the examiner's conclusion that it would have required undue experimentation to practice the claimed invention.

The examiner argues that "[t]he specification does not disclose which nucleotides . . . [are] essential . . . to make a representative number of DNA molecules with 90% homology to SEQ ID NO:1" (Answer, page 7) and the activity of AD7c-NTP, because "the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) [is] not well understood and [is] not predictable" (id., page 8).

In response, appellants point out that "[t]he specification provides exemplary methods for obtaining DNA molecules which are at least 90% homologous to SEQ ID NO:1. Such methods involve the isolation of DNA molecules from cDNA libraries by stringent hybridization techniques" (Brief, page 29). In addition, appellants argue that "[the] specification need not supply information that is well known in the art in order to satisfy the enablement requirement" (id., page 30), thus "methods that were well known in the art at the time of the effective filing date of the application would have been available to persons of ordinary skill in the art to obtain DNA molecules . . . at least 90%

homologous to SEQ ID NO: 1" (id.). Appellants argue that "[o]nce obtained, DNA molecules that are at least 90% homologous to SEQ ID NO: 1 could have easily been tested for the ability to encode a protein having an activity of AD7c-NTP" and "[t]he specification describes various methods for assaying for AD7c-NTP activity" (id., page 32). Appellants argue that neither the methods of obtaining DNA 90% homologous to SEQ ID NO: 1, nor the methods for determining whether they have AD7c-NTP activity "require knowledge of 'essential' nucleotides" (id., page 35), and "[a] skilled artisan would not have needed to predict the structural and/or functional consequences of particular mutations or base changes in order to produce [the claimed] DNA molecules" (id., page 36). We agree with appellants that "any uncertainty . . . associated with predicting protein function from sequence data is irrelevant" (id., page 37) in the context of the claimed invention. In view of the art-known methods of making DNA molecules at least 90% homologous to SEQ ID NO: 1 and the disclosed screening methods, the examiner has not adequately shown that more than routine experimentation would have bee required to practice the invention of claims 1-3, 5, 6 and 35.

With respect to claims 10-13 and 44-47, the examiner concludes that "the specification does not provide sufficient guidance for one skilled in the art to make and/or use the claimed . . . in vitro drug screening system" (Answer, page 9) because "the specification does not teach how to distinguish true negatives from false negative[s] or true positives from false positives" (id.), or "an increase in degradation of the protein . . . from a decrease [in] expression of the protein" (id.).

It may be, as the examiner argues, that there will be instances where "suppression or prevention of expression of the protein coded for by the DNA construct [ ] would reflect interaction [between the candidate drug and] the [heterologous] control sequence and result in false positives/false negatives" (Answer, page 9), and that it

may not be immediately apparent whether "the mechanism caused by the candidate drug is the result of interacting with the promoter, the cDNA, or another protein in the cultured cells" (id., page 10). Nevertheless, such criticisms of the claimed method are beside the point.

As appellants point out, "the claims are directed to methods for screening a candidate drug that is potentially useful for the treatment or prevention of Alzheimer's disease, neuroectodermal tumors, malignant astrocytomas, or glioblastomas" and "do not require that the drug identified by the claimed methods necessarily be effective for the treatment of Alzheimer's disease or other conditions" (Brief, page 44). We agree with appellants that the examiner has not established that claims 10-13 and 44-47 lack enablement on this basis.

In our view, the reasons cited in support of the examiner's rejection are insufficient to support the examiner's conclusion that the claims are not enabled by the specification. Accordingly, the rejection of claims 1-3, 5, 6, 10-13, 35 and 44-47 under the first paragraph of 35 U.S.C. § 112 is reversed.

AN ADDITIONAL ISSUE

The present specification indicates that polyclonal antibodies were used to isolate AD7c-NTP cDNA from an AD brain expression library, and that a clone, referred to as AD10-7, was deposited at the ATCC under accession no. 69262, and its sequence was published in Figure 16R of WO94/23756. In addition, the sequence of the same or a similar clone was set forth as SEQ ID NO: 120 in another publication, WO96/15272. Specification, page 5. The published sequences are said to comprise "numerous errors" (id.), nevertheless, appellants and the examiner may wish to consider whether claims encompassing DNA constructs "at least 90% homologous" to

SEQ ID NO:1 and coding for "a protein that has an activity of AD7c-NTP" are anticipated, or obvious over, these earlier deposits and/or descriptions of AD7c-NTP.

CONCLUSION

The rejections of the claims under the first paragraph of 35 U.S.C. § 112 as lacking written descriptive support and lacking enablement are reversed.

REVERSED

William F. Smith
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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Sterne, Kessler, Goldstein & Fox, PLLC
1100 New York Avenue, N.W.
Washington, D.C., 20005